Vaccination Scientifically Considered.

BY

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A Paper read before the Annual Meeting of the Association of Public Vaccinators of England and Wales at Leeds, on the 25th Oct., 1907.

Published by the Association of Public Vaccinators of England and Wales.

PRICE SIXPENCE.

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Diminished virulence of small-pox.

It is an indisputable fact that the ravages of small-pox have been diminished since the introduction of vaccinia. This improvement, described as a "casual coincidence" by Dr. A. R. Wallace, is attributed by him to improved sanitation, a larger consumption of fresh fruit and vegetables, and a more extended "use of tea and coffee" by the community. It is difficult to see how any of these factors could attenuate the virus of a disease which shows no regard for age, individual health, race, or social surroundings.

Death of Louis XV. from small-pox.

Illustrative of the latter point, Carlyle describes how in the spring of 1744 Louis XV., stricken with "confluent small-pox," has been carried home from little Trianon, and has been "put to bed in his own château of Versailles." His daughters the princesses alone wait at the loathsome sick-bed. The "putrid infection reaches even to the Oeil-de-Boeuf; so that more than 50 fall sick and 10 die." And on the 10th of May "the Louis that was lies forsaken, a mass of abhorred clay." As in-

stancing the ravages of small-pox in prevaccination days, one may quote the old-time proverb, "From small-pox and love few remain free."

Sanitation and small-pox.

With regard to the effect of sanitation on small-pox, Dr. M'Vail clearly points out that "the group of agencies to which, in the present day, the adjective sanitary is usually applied, such as improved water supply, improved excremental removal, increased living room, and better ventilation—have had their effect less in zymotics as a whole than in particular diseases like cholera, enteric fever, and typhus, the causes of which lie in the particular evils that these agencies are fitted to combat."

The proportion of mortality among children suffering from scarlet fever, measles, and whooping cough is almost the same now as it was 50 years ago, affording a remarkable contrast to small-pox. On the Registrar-General's authority the general death rate in England has decreased 9 per cent., while that of small-pox has fallen 72 per cent.

There is no reason, as Ernest Hart says, "why small-pox, apart from vaccination, should be affected to a greater extent by sanitation than, say, measles or whooping-cough. Yet during the same period that small-pox mortality has declined 72 per cent., that of measles has fallen only 9 per cent., and that of whooping-cough little more than 1 per cent."

Warrington epidemic.

As further disproving the influence that sanitation affects the distribution of small-pox, at Warrington during the epidemic of 1892-3, of the vaccinated children under 10 years, 4.4 per cent. had small-pox and 6 per cent. died. Among the unvaccinated of the same age period, 54.5 per cent. suffered the disease, and the death rate was 37.5 per cent. The incidence, therefore, is much greater among the unvaccinated than the vaccinated, yet both

classes were living under the same sanitary conditions in the same area.

Altered age incidence of small-pox since vaccination.

One of the most cogent arguments in favour of vaccination as a preventive measure is the change of the age incidence of small-pox since the systematic enforcement in 1871 of obligatory vaccination.

In prevaccination days, out of every 1,000 deaths due to variola 800 occurred in children under five years of age, but, as remarked by the Registrar-General in his 43rd annual report with reference to a table on this altered age incidence, "The figures show conclusively that coincidently with the gradual extension of the practice of vaccination there has been, in the first place, a gradual and notable decline in the mortality from small-pox at all ages ; in the second place, that this decline has been exclusively among persons under 10 years of age, and, most of all, among children under five years; thirdly, that after the age of 10 years the mortality, so far from having declined, has actually increased very slightly among persons from 10 to 15 years of age, but very greatly for persons older than this ; and, lastly, that the increase has been the greater the more advanced the time of life."

In seeking a cause for the diminished virulence of small-pox, a more satisfactory reason than sanitation would be, that the virus of small pox has gradually been attenuated by growth on a soil rendered relatively sterile by vaccination. If we compare syphilis as one sees it in our times with the accounts and models of the disease, of, say, Sir Astley Cooper's day, on the whole it is of a milder variety, and this mitigation of the disease is probably due to the fact that the syphilitic virus is being year by year attenuated by the systematic use of mercury.

Syphilis and vaccinia.

Having incidentally mentioned syphilis, I may point out that it has recently been shown by Neisser that the virus of this disease cannot live outside the body, however preserved, for more than 12 hours. It is, therefore, certain that syphilis cannot be conveyed by calf lymph as ordinarily procurable.

Principle of Jennerian vaccination.

The virulence of an organism can be lessened by passing it through the body of an animal of another species. Burdon Saunderson and Duguid discovered that they could diminish the virulence of the anthrax bacillus by passing it through guinea-pigs, and that after such passage anthrax was no longer fatal when inoculated in oxen. Pasteur found by inoculating from one rabbit to another, that the organism of swine-fever became more virulent for rabbits, but less so for the pig. If a pig was inoculated with the virus of swine fever which had been passed through a series of rabbits, it did not die, though it became ill. He further found that in a pig thus treated immunity was established for at least a year. We thus see that the passage of a virus of a disease in one animal through the body of an animal of another species may bring about its attenuation. The attenuation of small-pox and its conversion into a mitigated form of variola, namely, vaccinia, by passage through a series of calves is, therefore, not singular, but depends on a well-established principle.

As there is no evidence that one disease is able to confer immunity from another disease, it becomes necessary to establish the identity of the virus of vaccinia and variola. This practically resolves itself into the question of the relationship of cow-pox to small-pox. It is about this point

Relationship of cow-pox to small-pox.

that so much controversy has arisen. We have, therefore, to decide what happens when a calf is inoculated with the virus of small-pox. According to Chauveau nothing happens, but it must be remembered that Chauveau used grown cows. Dr. W. J. Simpson, in 1885, using a cow, was more successful, and after passing the virus through a series of calves, about 1,500 children were vaccinated with this lymph with conspicuous success.

Klein, Hime, and Copeman, by scraping the lymph from the very slight reaction induced in the variolated calf, and subsequently passing it through a series of calves, succeeded in obtaining a virus of attenuated though constant virulence, exactly as Pasteur obtained a constant though attenuated virus of hydrophobia by passage through a series of monkeys.

King's experiments.

Surgeon-Major W. G. King, of the Indian Medical Service, gives the following account of the conversion, or, more correctly speaking, of the attenuation, of small-pox into vaccine virus, which is so lucid that I cannot do better than quote his own words. After stating that he secured a certificate from the principal residents in the village from which it was obtained, that the lymph was actually taken from a child suffering from small-pox, he says: "The calf inoculated with this lymph was a young bull. Both lines and punctures were employed on and near the scrotum. For the first three days there was every appearance of local results at the points of insertion. I then noticed on the scrotum, about one-quarter-inch from the inoculated line, a firm, broad papule arising. My belief is that it was a secondary vesicle, but as it was close to the site of the original punctures I was left in doubt, but so far as examination would prove the fact, there was no sign of a puncture having been made at the point.

Lymph was taken from this papule just on its verging into the vesicular stage, and was used for calf No. 2. In the meantime a crop of secondary papules appeared on the perineum, where there was not the slightest doubt as to there having been no inoculation effected. Another papule also appeared on the thigh. From lymph expressed from these, I inoculated calf No. 3.

The papules found at the original site of inoculation of the small-pox virus in calf No. 1 now aborted and completely disappeared—the secondary eruption, however, continued its course. In the first and second calves again distinct secondary eruptions appeared. A transfer to a buffalo conveyed by the first—the doubtful secondary vesicle—produced no result, although the crop in calf No. 2 was very favourable. *I have thus the lymph from the true secondary vesicle only in operation.* The third calf has now no secondary eruption, and the general appearance is identical with true benign vaccine lymph. (This calf, however, subsequently developed a secondary eruption.)

Finally calf No. 1—which I would remind you was that inoculated direct with small-pox virus—was inoculated seven days after the appearance of the secondary small-pox vesicles with ordinary fresh animal lymph, and the result is nil, showing, I think conclusively, that vaccine and small-pox virus are one and the same, and that Jenner's contention, that vaccinia is but small-pox modified by transmission through the cow, is absolutely correct." He passed his lymph through a further series of four calves, and mentions later that he issued vaccine from the small-pox lymph modified by transmission as described for about 3,000 cases daily, and did not hear of a single untoward result therefrom in the human subject; while on the calves used for its preparation the vesicles were typical in their course and character. He also points out the

Effect of late lymph.

influence of late lymph on the system, and emphasises the importance of seeing that clear lymph (generally about the 96th hour from the calf) only is used, for if used after this date he found that local inflammatory reaction was very high. This is exactly comparable to what occurs in small-pox, and is due to the pyogenic organisms resident on the skin gaining an entrance into the vesicle and there multiplying. This point will be referred to again, as it has a most important bearing on the prevention of the occurrence of ulceration and other vaccinal injuries in man.

As it has been asserted that all the experiments on the variolisation of calves have been done in vaccine establishments, it has been contended that what really took place in these experiments was that the calves were not infected with small-pox virus at all, but with vaccine—that is, cow-pox virus. Elaborate precautions were taken in all recent experiments to avoid this occurrence, and it would, therefore, be more than singular for such a contingency to have taken place on each occasion. With regard to this point, Dr. W. J. Simpson informs me that his experiments in Aberdeen on the variolisation of cows and calves in 1885 were made inside the premises of the small-pox or infectious hospital, thus clearly showing that a vaccine establishment is not a necessary accompaniment to the variolisation of the calf.

Creighton's arguments.

Because the effect on a child's arm is, on the whole, the same as on a milker's hand—namely, an ulcer, as the result of the experimental infection with cow-pox, and not a typical vaccinia vesicle—it does not follow that this result is due to the specific organism of cow-pox, either on the hand of the milker or on the arm of the child.

Neither is the supervention of a macular roseola rash, lichen or dry papules, or vesicles in the form of pemphigoid

bullæ in a child thus vaccinated, as stated by Creighton, necessarily due to the specific agent. When we consider that the cow-pox lymph was collected in former times without due regard to surgical cleanliness, it must be obvious to anyone with a knowledge of bacteriology that the lymph collected in this manner may easily have contained a number of micro-organisms, pus-producing and other bacteria, from which the specific agent of cow-pox may have been absent. It is, therefore, not logical to ascribe certain phenomena to the action of a virus which is not a pure culture. Jenner's rule was to take the matter for vaccination before the areola appears. If a vesicle be emptied after that period, he found the lymph from it apt to cause ulceration.

Cause of ulceration.

We now know the reason for this observation is that the lymph of Jenner's day had not been freed before use from pus-producing and other bacteria, and, what is equally important, neither had the skin at the site of insertion at the time of vaccination been freed from those pyogenic cocci —such as the staphylococcus pyogenes, albus, &c., normally resident on it.

These bacterial denizens of the skin, at a certain stage in the development of the pock, gain an entrance through the lesion of the pock, and set up brawny swelling. Should these bacteria, once within the vesicle, find their way through the incompletely cornefied cells of the rete of the healing pock, diffuse cellulitis and extensive ulceration may occur. It has, therefore, not been proved, as Creighton says, that "cow-pox might be *easily* cultivated back to its original type"; for it requires great care to maintain the pure cultivation.

It cannot, therefore, be urged too strongly, that the skin should be rendered as aseptic as possible at the site of inoculation before introducing the vaccine. The lymph at

present supplied you, being thoroughly sterilised by chloroform vapour, any vaccinal accidents which may supervene will be either due to the neglect of surgical cleanliness at the time of vaccination, or to the subsequent infection of the pock with dirt from the patient's fingers, &c. We think so much of the "germs" nowadays that we often forget all about the soil, the tissues of our patients. A germ of low virulence which could not flourish in a healthy patient may easily prove disastrous to a weakly child. It is wiser, therefore, either to postpone or entirely exempt from vaccination a weakly or sickly infant, not because of the direct effect of the vaccine virus itself, but because of the want of resistance in such a patient to suppurative organisms which may invade the pock after the vaccination.

I have shown that in small-pox the pock is absolutely sterile on all culture media up to the seventh day of the eruption. On this day various pus-producing staphylococci resident on the skin, gain an entrance into the pock, cause suppuration, and the supervention of the secondary fever. This epiphenomenon is preventible if the skin of a small-pox patient is freed from these pyogenic bacteria during the period of eruption by the free use of antiseptics. The same line of argument applies to the risks stated by Creighton to be inherent in the cow-pox infection, such as erysipelas, jaundice, skin eruptions, vaccinal ulcers, and so-called vaccinal syphilis. All these are stated to be inherent in the virus; but what about the risk contingent to the puncture of the skin or subsequent infection of the pock with dirt? As Dr. Draper, of New York, tersely puts it, "Men are ever prone to mistake coincidences for causes." As a matter of fact, all these diseases or signs are not due to the vaccinia virus itself, are not peculiar to vaccination, and may result from any infected wound to which adventitious bacteria, variously derived as above stated, have gained access.

The theories of immunity.

Side-chain theory.

According to Ehrlich's side-chain theory of acquired immunity, a molecule of protoplasm may be considered as consisting of an executive centre, and a number of side-chains which have an affinity for foodstuffs: bacteria and their toxins can be included in this category. When a toxin is introduced into the system of an animal, the *receptors* or side-chains of the tissue elements which have an affinity for it, enter into chemical combination with the *haptophore*, *i.e.*, binding side-chain of the toxin. This combination being of a firm nature, the receptors thus affected are lost to the cell. New receptors are formed by the cells to replace those lost. The advent of fresh toxin stimulates the cells to produce more and more receptors. This leads to excessive formation of receptors, provided the health of the cells is not too much impaired by the toxin to allow of their formation.

Three orders of receptors thus arise; these, when separated from the cells pass into the blood serum and constitute three orders of anti-substances. The first kind, to which anti-toxin and anti-ferments belong, merely combine with the substance which has provoked its formation, without producing any observable alteration in it. In the second kind, of which agglutinins are instances, the anti-substance may occasion visible change in the substance, *e.g.*, clumping of bacteria. In the third class of anti-substances, known as *immune bodies* or *amboceptors*, in addition to combination with the substance, they bring about the junction of a normal constituent of the serum, namely, the *alexine* or *complement*, which causes solution or death of the substance, *e.g.*, lysogenesis of bacteria.

The second and third classes of anti-substances are generally developed in response to the injection of formed elements, such as blood, bacteria, &c. From the fact that

a toxin may lose much of its toxic effects and yet combine with the same proportion of anti-toxin molecules, Ehrlich concludes that a toxin possesses two combining groups. One, the *haptophore* group, the connecting link between the toxin and the corresponding *haptophile* group of the cells. The second, the *toxophore* or poisoning group, which can only unite with the cell after the affinity of its first or combining group is satisfied.

By the following experiment the existence and relationship of these two groups are made manifest. If an animal be injected with tetanus toxin the receptor groups of the central nervous system fix the poison within a few minutes, for, though the animal be bled almost immediately and transfused with fresh blood from another healthy animal, it nevertheless dies of tetanus, though symptoms do not supervene for 24 hours. It is during this period that the combination of the *toxophore* or poisoning groups of the toxin and the toxophile groups of the cells occur, and, when complete, the signs and symptoms of tetanus poisoning become apparent.

Applying the above theory to explain the insusceptibility of a person, who either, by reason of a previous attack of small-pox or vaccination is immune to re-infection, we may assume that the serum of such a person contains anti-small-pox substances, which, when they meet with the re-introduced virus of small-pox, be its nature protozoan or bacterial, so affect it, in the direction of agglutination, lysogenesis, or increased opsonic action, as to destroy its vitality.

Alexocyte theory.

Another view of the way in which a previous attack of a disease protects against a second infection may be termed the alexocyte theory. According to this view the leucocytes secrete or themselves dissolve into germicidal pro-

teids and nucleins, termed alexins; these so affect the micro-organisms that the phagocytes are able to destroy them.

That the phagocytes can be schooled the better to accomplish this function is shown by the fact that while in an ordinary rabbit infected with anthrax moderate phagocytosis and death follow, in rabbits previously vaccinated active phagocytosis and recovery take place. The phagocytes of a vaccinated animal, having, as it were, learnt their lesson, can effectively combat the attacking germ. I incline to the view that it is chiefly through the education of the phagocytes that vaccinia or a previous attack of small-pox protects against re-infection. In a person susceptible to small-pox I think the aetiological agent, whatever its nature may be, does not attract, but rather repels the phagocytes; in other words, negative chemotaxis occurs. In consequence, the germs multiply and infect the system from a situation (namely, the prickle area of the skin) difficult of access to the phagocytes. On the other hand, in a person immune to vaccinia or small-pox, the moment the virus is introduced into the body, owing to the trained state of the leucocytes, positive chemotaxis supervenes, the leucocytes are attracted to the virus, secrete alexins, and soon destroy it.

The following are some of the reasons for this view. The only tissues of the rabbit where the virus of vaccinia can multiply are the skin and cornea, provided that the insertion of the virus be done with the very slightest injury to these tissues. The process can be watched in the cornea, and whether we agree with Guarnieri that the changes in the corneal cells are due to the development of his parasite, the *cytoryctes variolæ*, or whether we think that the appearances are due to degenerative changes in the cells, there is no doubt that leucocytes do not approach the field of activity. We know by experience that in

vaccination, especially in re-vaccination, we are more likely to succeed if we draw little or no blood, for in spilling blood we free a number of leucocytes which, owing to injury, secrete or dissolve into alexins, and thus may help to destroy the virus.

Calmette and Guerin's experiments on rabbits.

Calmette and Guerin found in vaccinating the rabbit that if the skin be much wounded, or the slightest effusion of blood occur in the field of operation, the insertion of the vaccine fails. They also found that, however the virus was introduced into the body of this animal, whether into the veins or dusted as a powder in the nose, or injected into the trachea, immunity was established about the sixth day, though no eruption was produced; but that for the implantation and evolution of the vaccine virus very slight skin lesions were absolutely necessary. They experienced that if the virus was introduced into a rabbit's peritoneal cavity, previously prepared by an injection of broth so as to provoke the formation of an exudate, the recovered virus was found to be free from bacteria. The leucocytes had caused the adventitious bacteria in the lymph to disappear, but respected to some extent the vaccine elements—certain refringent motile grains present in the lymph. No organ in the body was found capable of conveying the virus to a second animal or of conferring immunity. From which they infer that the vaccine virus does not appear able to grow or multiply in any organ where the leucocytes have access. As regards the period when immunity is established in man, Cory concluded that immunity was established on the ninth day. For if vaccination be done by a single insertion on eleven successive days, those made after the ninth day do not develop. It would appear, therefore, that immunity is not conferred until the pocks have reached their full development, for during the week following

vaccination the patient may be successfully re-vaccinated, and may also contract small-pox. On the other hand, if a person has been exposed to the infection of small-pox and is vaccinated within 70 hours of such exposure, he may escape small-pox. It may be asked, however, if the neutralisation of the active agent may not be due to some germicidal constituent of the serum. I think not; for if one takes the serum of a person immune to small-pox and vaccinia, and introduces into such a serum some calf lymph, washed to free it from the glycerin, certain small refringent grains, already alluded to, will be found to be actively motile (that this activity is not a molecular vibration can be proved by adding a small quantity of a perchloride of mercury solution, when all movements of the particles cease). In such a preparation no clumping or agglutination, no solution or lysogenesis of these refringent granules takes place. One or the other phenomenon would assuredly occur if these granules were, as I think (a view Calmette and Guerin support) the active agent of small-pox and vaccinia, and if the serum contained an anti-substance.

Histological changes in variola and vaccinia.

There are no observable differences in the minute changes occurring in the skin in variola and vaccinia. The first observable change is a dilatation of the lymph channels between the cells of the deeper layers of the rete malpighii, which communicate with the enlarged lymph spaces of the corium immediately beneath the site of the commencing vesicle. Some cells in the mesial prickle area will be noticed to stain more faintly; their nuclei, though persistent, are not so distinct as those of the cells in their vicinity. At this spot the vesicle is about to develop, vacuoles appear in the cytoplasm of these cells, run together, and leave the nucleus isolated save for some delicate strands connecting it to the cell wall. To this reticulated appearance of the cells, Unna

has given the name of reticular colliquation. Deeper down in the rete ballooning colliquation of some cells occurs. In these a developing vesicle distends the affected cell, and gradually pushes the nucleus against the side of practically all that remains of the cell, namely a very thin cell wall. Superficially the cells of the granular layer become more numerous, and may persist to quite a late stage in the vesicle formation.

Liquefaction of the cells which have undergone reticular colliquation now takes place, and a small cavity, across which stretch strands of cells that have escaped reticular colliquation, is thus formed. Lymph collects in this the early stage of the vesicle which now encroaches on the granular and corneous layers superficial to it.

The cells, especially those on its inferior and lateral aspects, surrounding the area where these changes take place, undergo active proliferation. The lymphatics and neighbouring blood-vessels, especially as to their adventitia, are crowded with plasma cells, provided the virus of small-pox or vaccinia alone be present. If bacteria are present, polymorphonuclear leucocytes will be found as well. This proves that the contents of a vaccinia or small pock does not contain *matter*, by which we understand morphosed polymorphonuclear leucocytes.

Through the courtesy of Dr. E. C. Greenwood I had the opportunity of examining the contents of several vaccinia vesicles on the ninth day in patients of his, and found the contents absolutely sterile on all ordinary media, and polymorphonuclear leucocytes practically absent.

In some accounts of these histological changes you will read a somewhat different description. It seems to me that in these accounts, two distinct phenomena, each of which is provoked by a different agent, are described as though attributable to the virus of small-pox. The vesicle is described as being filled with white corpuscles. I be-

lieve this appearance in the vesicle is due to the presence of pyogenic organisms, is occasioned by these organisms, is in no wise due to the specific agent of small-pox and vaccinia, and that when the latter is alone present, no infiltration with polynuclear leucocytes takes place. I may seem to labour this point somewhat, but the practical import of this recognition would have saved vaccine virus from being called foul matter, an excitant of ulceration and other horrors of which it is absolutely innocent, and is incapable *per se* of provoking.

Lying between the epithelial cells and between the connective tissue bundles of the hypoderm, certain darkly staining bodies about four times the size of a coccus may be seen. Situated as they are outside the area of nuclear fragmentation, they cannot be fragments of nuclei, their nature is uncertain, and they are considered by some observers to be protozoa. From the foregoing description it will be seen that the cavity of the pock is unilocular, being divided by incomplete dissepiments of altered epithelial cells, so that it is not correct to speak of it as a multilocular cavity. It will also be observed that at a time when the pock appears as a papule there is within it a commencing vesicle.

Umbilication.

Umbilication is chiefly due to two factors, though a third may be operative. The later umbilication is no doubt due to the absorption of lymph from the pock and to the presence of a hair follicle. As the corneous layer is more firmly attached to the sheath of the hair than elsewhere, the vesicle cannot expand in this direction, and the result is that the vesicle is blown out about the hair as a depressed centre. Early umbilication is probably due to the fact that the periphery of the pock is better supported by the underlying cells than its centre; the centre, therefore, caves in somewhat in this region.

Repair.

The cavity of the pock gradually comes to occupy a relatively superficial position, being pushed upwards by the continued multiplication of the deeper cells of the rete. The upper cells of this regenerating layer next undergo cornification, and thus the pock is gradually shut off from the subjacent tissues. This cornifying process proceeds from without inwards, so that the central inferior portion of the pock is the last excluded. If, as before indicated, organisms gain entrance to the pock, they can enter the tissues beneath, through this opening, and give rise to ulceration and subsequent scarring.

The aetiological agent of small-pox and vaccinia.

Bi-polar Bacillus.

Klein and Copeman have described a minute bipolar-staining bacillus as occurring in vaccine lymph. It is necessary for the organism to be spore-bearing, otherwise it would be killed by the chloroform vapour now used in the sterilisation of calf lymph. For spores alone have been found capable of resisting this treatment. The majority of present-day observers deny the presence of any form of bacterium, and certainly the histological appearances of the pock and the peculiar properties of lymph seem to be opposed to a bacterium as the causative agent.

Cytoryctes variolæ.

Guarnieri was the first to advance the view that a sporozoon, that is, an intracellular protozoon, is the active agent in vaccinia and small-pox. Councilman, Magrath, Brinckerhoff, and Calkins, in America, have published an extensive research on the Cytoryctes variolæ Guarnieri. According to Councilman, the difference between small-pox and vaccinia lies in the fact that in the former there are two stages in the development of the sporozoon. One stage occurs in the cell substance, while the other takes

place within the cell nucleus. In vaccinia the intranuclear stage does not occur. The opponents of this view state that the appearances described are really degenerative changes in the cell, and are not due to a parasite. One can readily conceive that in dealing with such small bodies dependence on entirely morphological appearances may easily lead to error.

A third view was first advanced by Funk in 1901 and further investigated by myself in 1904. According to us, the causative organism is a comparatively large protozoon, the "sporidium vaccinale" which can easily be seen. I believe that the refringent motile granules, which constitute so great a portion of calf lymph, are spores freed by this sporidium This sporidium has been regarded in turn as nothing but a leucocyte, a dead epithelial cell, and, lastly, as some fatty body.

Sporidium vaccinale.

One thing is certain; it cannot be all three of them. The fact remains, that given a sample of calf lymph, the more sporidia and spores are present, the more active you will find the lymph.

Printed by KING, SELL, & OLDING, Ltd., 27, Chancery Lane, London, W.C.